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PAPER READ BEFORE THE AMERICAN SURGICAL ASSOCIATION.

By N. SENN, M.D., Ph.D., LL.D.,

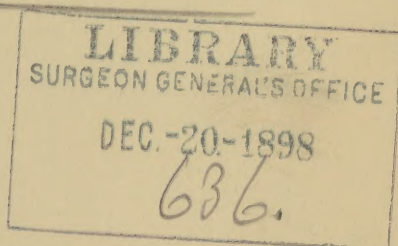
Professor of Surgery in the Rush Medical College; Attending Surgeon Presbyterian Hospital, and Surgeon-in-Chief St. Joseph's Hospital, Chicago, Illinois.

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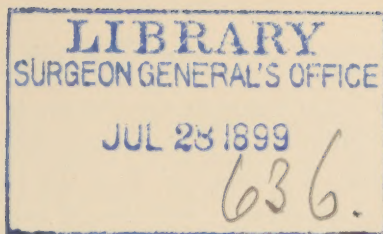
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*presented by the author*







## THE ETIOLOGY AND CLASSIFICATION OF CYSTITIS.

PAPER READ BEFORE THE AMERICAN SURGICAL ASSOCIATION.

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GENTLEMEN,—The bladder is the dilated portion of the urinary tract interposed between the ureters and the urethra, and in a normal condition serves as a temporary reservoir for the urine. It is composed, like all receptacles of this kind, of three anatomically and physiologically distinct coats,—(1) mucous coat, (2) muscular coat, and (3) peritoneal coat. The mucous coat differs from the structures of this kind as found in most other organs in that it contains no glandular appendages. The mucous membrane of the urinary bladder is devoid of glands, and is made up of several layers of squamous epithelium. The fibres of the muscular coat are arranged in such a manner that when they contract, the organ being in a normal physiological condition, complete evacuation of its contents takes place, while during the intervals between urination they permit insensible painless distention to the physiological limits. The serous coat, like all peritoneal investments of other abdominal organs, is admirably adapted to insure free mobility of the organ in the performance of its complicated functions. The bladder is freely supplied with blood-vessels, which take such an important part in all inflammatory processes. The lymphatic vessels are found only in the muscular coat, and play an important rôle in the pathology of interstitial cystitis and in the extension of infective processes to and from the bladder.

### ABSORPTION FROM THE BLADDER.

In the study of inflammatory affections of the bladder it is important to obtain a clear conception of the function of its mucous



lining. The epithelial lining of the bladder is not, properly speaking, a mucous membrane, as it is not supplied with glands and in a normal state secretes no mucus. It is the reservoir for an excretion and not for a secretion. For this, if for no other reason, we should *a priori* question its ability to absorb medicinal and toxic substances. The mucosa of the bladder contains no lymphatics; it lacks, therefore, all the physiological elements necessary for absorption. Gerota (*Anatomische Anzeiger*, Band xii., p. 347), in the examination of more than sixty bladders, could not demonstrate, either macroscopically or microscopically, the presence of lymphatic vessels belonging to the mucous membrane. None could be detected in the trigonum. The few vessels found in the submucosa of the vesical neck were identified as the lymphatics of the urethra, which extend for a short distance into the neck of the bladder, but soon enter into the muscular coat. That the normal mucous membrane of the bladder is not an absorbing surface has been demonstrated by the clinical observations of Civiale and many other surgeons and the experimental work of many investigators, among them Kuss, Susiné, Alapy, Alling, Lewin and Goldschmidt, Caze-neuve, and Livon.

Guyon is of the opinion that the vesical mucous membrane lacks the function to absorb, while Bazy and Sabatier are of the opposite belief.

Hottinger's ("Zur Frage der Absorptionsfähigkeit der gesunden Harnblase," *Centralblatt für die Krankheiten der Sexual-Organ*e, Band vii., Heft 5) experiments seem to prove that enormous quantities of poison must be introduced into the bladder of animals to produce death. Death in such cases he attributes to a process of diffusion rather than of absorption.

Lewin and Goldschmidt ("Die Resorption Körperfremder Stoffe aus der Harnblase," *Archiv für Experimentelle Pathologie*, December 30, 1895) made many experiments on animals, and came to the conclusion that the healthy mucous membrane of the bladder is impermeable to toxic substances, and when absorption does take place it is from the prostatic portion. Their experiments were made by ligating the neck of the bladder and injecting the solution directly into the bladder through an abdominal incision.

Alapy ("Ueber das Absorptionsvermögen der Harnblase," *Centralblatt für die Krankheiten der Harn- und Sexual-Organ*e, 1895,

Band vi., Heft 4 and 5) experimented with strychnine and obtained very variable results. With a view of explaining these differences in the results, he made a further series of experiments with cyanide of potassium. All of the animals thus treated died. He concluded from his experiments that when a non-volatile poison is used and the results are not constant, the positive results followed the absorption of the poison from the prostatic portion, while no absorption occurred from the vesical mucous membrane, and that death resulted in those male animals in which the poison escaped from the bladder through the urethra.

Recently Ashdown has succeeded in killing rabbits by injecting poisonous substances into the bladder.

Bazy and Mazon, from repetition of the same experiments, came to the conclusion that poisonous substances in solution are absorbed by the intact vesical mucous membrane. It is more than possible that in these experiments absorption took place not from the mucous membrane of the bladder, but by the escape of fluid into and absorption from the urethra. From a practical stand-point it is safe to assume that the intact mucous membrane of the bladder is a non-absorbing surface, and that when absorption does take place it is in consequence of injuries and lesions which open up avenues for the entrance of toxic and infective substances into the lymphatics or blood-vessels of the middle coat.

A rational discussion of the diagnosis, prognosis, and treatment of cystitis must be based almost entirely on what we know concerning the etiology and classification of this very variable and obstinate disease. I have deemed it expedient and advisable to limit my remarks on this occasion to the etiology and classification of cystitis, with the expectation that it may serve the purpose of preparing the way for a more general and thorough discussion of the more purely surgical aspects of this disease at our next or some subsequent meeting.

## I. ETIOLOGY.

The recent great advancements in the prevention and more successful treatment of infective surgical diseases are the direct outcome of the vast increase of our knowledge concerning their etiology. Surgical bacteriology paved the way for rational surgery. It is now very generally conceded that inflammation of any tissue



or organ is invariably caused by microbial invasion, and that all other causes only act by determining or favoring infection. If this be true, it is apparent that the successful treatment of cystitis presupposes an accurate knowledge of the nature of the microbial origin of the inflammation. Suppurative cystitis and tubercular cystitis are so entirely different in the nature of their bacteriologic origin that the method of treatment successful in one would almost with certainty aggravate the other. Inflammation of the bladder is often the result of a mixed infection, and it is of paramount importance in all such cases to gain accurate information by bacteriologic examination of the urine concerning the part which each kind of microbes plays in the causation and continuance of the inflammatory lesion before an intelligent and successful course of treatment can be devised and carried into effect. It is of special importance in the successful management of cystitis and conditions mimicking cystitis clinically to make a sharp distinction between the cases in which the symptoms are caused by inflammation and those in which they are due to non-inflammatory pathological conditions. It will be seen from these remarks that the modern etiologic study of cystitis is based largely on a carefully conducted bacteriologic examination of the urine. The exercise of patience and perseverance is often required, as in many cases the urine has to be examined repeatedly before the necessary information is gained.

(a) *Predisposing Causes*.—In our old text-books we find in the discussion of the etiology of disease the familiar distinction made between predisposing and exciting causes. In our modern literature we find all the exciting causes discussed under the head of predisposing causes, and the list of exciting causes is an entirely new one, containing terms unknown to medical and surgical writers of less than fifty years ago. As predisposing causes of cystitis we recognize and describe such injuries, agencies, and influences as are concerned in establishing a *locus minoris resistentiae* in the tissues of the bladder in which a sufficient number of pathogenic microbes of adequate virulence accumulate to produce those tissue changes which characterize inflammation. The injured tissues or contents of the bladder furnish the necessary nutrient medium in which the microbes grow and multiply. All of the predisposing causes do one of two things or both: 1. They effect tissue changes which determine the localization of microbes from the bladder, adjacent organs,

or the general circulation. 2. They furnish a nutrient medium for the growth and multiplication of microbes.

*Retention of Urine.*—The most frequent of all predisposing causes of cystitis is retention of urine from any cause. Retention of urine acts in two ways in predisposing the bladder to infection: 1. The retained urine serves as a culture medium for some of the microbes which are known to produce cystitis. 2. The distended bladder wall is subjected to pressure which in itself is a potent predisposing influence.

Mesnil de Rochemont ("Zur Pathogenese der Blasenentzündung," Leipzig, 1896) made experiments with a view of demonstrating that the presence of pathogenic bacteria in the bladder is not sufficient to produce cystitis, but that a second factor is necessary to induce inflammation which he has found in a disposition in the bladder wall. He made a bacteriological examination of the urine in twenty-five cases of cystitis. The urine was removed from the bladder under strict aseptic precautions. From these cases he cultivated from the urine fourteen different kinds of microbes. Of these microbes there were nine species facultative anaërobic and five obligate aërobic. One-half of them decomposed the urea; the remainder had no such effect. With the exception of one, all proved pyogenic in the animals experimented upon. He found that sterile foreign bodies inserted into the bladder and causing no obstruction never produced inflammation of the mucous membrane. The experiments with pure cultures were made by introducing the microbes into the bladder from above. His experiments also proved that the presence in the bladder of obligate anaërobic or facultative anaërobic microbes did not produce cystitis whether they did or did not decompose the urine. If, however, the urethra was obstructed at the neck of the bladder for twenty-four hours and the urine accumulated during this time, the presence of facultative anaërobic microbes, regardless of their effect on urea, caused cystitis, the urine remaining acid, while the presence of obligate aërobic microbes, on the other hand, which produced at the same time urea decomposition inserted into the bladder under the same conditions, caused ammoniacal suppurative cystitis. A temporary obstruction of the urethra without infection of the bladder according to duration produced hyperæmia, hemorrhages, and even necrosis.

The local effect of the toxic and irritating substances formed by



the action of some of the microbes on the urea of the retained or residual urine constitutes an additional element in the causation and propagation of inflammatory processes in the bladder. The gravest cases of cystitis occur in patients suffering from acute retention of urine in the event of the bladder becoming infected by careless catheterization, or otherwise. It is in such instances, more especially if the bladder is at the same time paralyzed, that the inflammation attacks almost from the very beginning the whole surface of the mucous membrane, and is so prone to extend along the ureters to the pelves of the kidneys. In cases of gradually increasing obstruction to the free outflow of urine, so frequently seen in neglected cases of stricture of the urethra and in prostatic patients, the residual urine plays an important rôle in the origin and extension of inflammatory affections of the bladder. It is in cases of cystitis with such a mode of origin that the trigonum of the bladder is almost constantly the starting-point of the infection and the inflammation following it. It is time that the medical profession should realize the well-known clinical fact that retention of urine is one of the most frequent and potent conditions in increasing the receptivity of the bladder to infection, and that cystitis can be most effectively guarded against by preventing the accumulation of urine in the bladder beyond the physiological limits. Knowing the great susceptibility of the bladder to infection when the urine is retained, it becomes the surgeon's duty to employ the strictest aseptic precautions in the evacuation of the organ by catheterization, puncture, or incision.

*Unrest of the Bladder.*—Abnormally increased muscular action of the bladder, as occurs in cases of central or peripheral irritation of the nerves which preside over the muscular structure of this organ, or in consequence of the action of local irritants, as stone, foreign bodies, tumors, chemical or toxic substances, is a recognized predisposing cause of inflammation of the bladder. The same may be said of reflex influences from adjacent organs, which exert a similar influence in increasing the function of the muscular fibres beyond the physiological requirements. Exaggerated muscular contractions of the bladder favor infection by the vascular changes which they produce, and especially by inducing the surgeon so often to resort to unnecessary harmful instrumental examination.

*Abnormal Urine.*—Abnormal conditions affecting the quality



or quantity of urine frequently precede inflammation of the bladder, and must be regarded in the light of predisposing causes. Hyperacidity or, more frequently, alkalinity of the urine, by causing congestion of the vesical mucous membrane and by disturbing the function of the bladder, furnish the conditions for a subsequent infection. Albuminuria, polyuria, and especially diabetes appear to increase the susceptibility of the bladder to infection. The elimination through the urine of irritants such as cantharides, turpentine, and allied drugs, and the irritating principles of certain articles of food and certain alcoholic beverages, produces alterations in the mucous membrane of the bladder which prepare the tissues for infection and inflammation.

*Tumors.*—Tumors of the bladder, malignant and benign, frequently precede and complicate cystitis. Vesical tumors may prepare the bladder in different ways for infection. They may cause retention of urine, vesical tenesmus, hemorrhage into the bladder, and, in the event of ulceration, the urine comes in contact with an abnormal surface, all conditions which would be favorable to infection. Again, tumors of the bladder are productive of symptoms which lead the surgeon frequently to explore its interior by the use of instruments, a method of examination to which the date of infection can be so often traced.

*Calculus and Foreign Bodies.*—The presence of a stone in the bladder is attended by symptoms which point to inflammation of the neck of the bladder minus the evidences revealed by a microscopic examination of the urine. It has been shown experimentally that the presence of foreign bodies in the bladder never produces inflammation independently of pathogenic microbes. A calculus or a foreign body becomes a predisposing cause of cystitis by the production of local lesions and vascular changes favorable to the localization and growth of bacteria, which are the essential cause of the inflammation. It is well known that a stone may remain in the bladder for years without causing cystitis, and the cystitis which so often complicates such cases can, in the majority of instances, be traced to instrumental examination.

*Pressure.*—Compression of the bladder from within and from without is a potent predisposing cause of cystitis. Pressure from either direction diminishes the vascularity and nutrition of the bladder wall, and in this way increases the susceptibility of the

tissues to invasion by disease-producing micro-organisms. This predisposing cause is most frequently met with in connection with cystitis in pregnant and puerperal women and in cases of myofibroma of the uterus, in which the tumor makes pressure against the bladder. It is in such instances that the infection is likely to extend from the surface to the underlying connective tissue, and that the subsequent inflammation often terminates in extensive exfoliation. An enlarged prostate may so encroach upon the bladder as to cause sufficient pressure to become a predisposing cause aside from the secondary lesions resulting from the chronic obstruction.

*Exposure to Cold.*—Sudden chilling of the surface of the body results in congestion of internal organs, which occasionally affects the bladder sufficiently to effect vascular changes, and they in turn determine an infection which otherwise would not have occurred. The embarrassed circulation in the vessels of the bladder is then to be considered as the direct cause of the localization of pathogenic microbes in this organ sufficient in quantity and virulence to produce an inflammation. In the absence of microbes in the bladder, adjacent organs, or the general circulation, no amount of exposure to cold can cause a cystitis.

*Venous Stasis.*—We have already mentioned as local predisposing causes of cystitis conditions which produce congestion, and have regarded them as predisposing causes. Venous stasis in the vessels of the bladder from more distant causes acts in a similar manner and is followed by the same results. Among such remote causes which disturb the circulation in the vessels of the mucous membrane of the bladder must be mentioned general enfeeblement of the circulation from different debilitating causes, organic heart-disease, consolidation or compression of the lungs, and cirrhosis of the liver.

*Trauma.*—To trauma has been assigned for centuries a direct influence in the causation of cystitis. Since it has been made clear that no inflammation is possible without infection, trauma has been transferred to the list of predisposing causes in the etiology of inflammation of the bladder as well as of any other organ. Trauma of the bladder from injury, the presence of foreign substances, or the action of chemical, toxic, or thermal influences creates a *locus minoris resistentiæ* for the localization of pathogenic microbes, or opens a pathway for their entrance from the bladder into the tissues



composing the bladder wall. Considered in this light, trauma in its various forms constitutes an important element in the causation of cystitis. The injection or instillation into the bladder of caustic solutions strong enough to damage the epithelial lining of the bladder has often provoked a cystitis which without such therapeutic intervention would never have occurred. The trauma inflicted by the passage of instruments into the bladder in search of stone or foreign bodies has undoubtedly been often responsible for similar disastrous results. Operations upon the bladder by either the suprapubic or perineal route have occasionally been followed by septic cystitis from infection during or after the operation, when the interior of the bladder before the operative intervention was in an aseptic condition. Contusion or laceration of the bladder resulting from the application of force from without or within never gives rise to cystitis unless the accident is followed by infection, either by the introduction of microbes by catheterization or the localization of microbes from the blood in the parts injured.

(b) *Exciting Causes.*—The essential or exciting cause of cystitis is invariably the presence and pathogenic action of microbes in the tissues of the bladder, the seat of inflammation. In the study of the etiology of cystitis it is important to consider in detail the routes of infection. From a practical stand-point it is well to admit that pathogenic microbes reach the interior of the bladder most frequently through the urethra by the use of instruments, or spontaneously by the extension of infective processes from the mucous membrane of the urethra to that of the bladder by continuity of surface. It is, however, well to remember that microbes may and do reach the bladder by other routes,—namely, through the urine from the kidney, the general circulation, and adjacent infected organs through the lymphatic channels. The study of the etiologic relationship of bacteria to cystitis dates back to a little more than ten years, and during this time sufficient proof has been accumulated to show that inflammation of the bladder is always the result of bacterial invasion. It was soon found that the disease may be produced by any microbe which possesses pyogenic properties.

Bumm ("Die Actiologie des puerperalen Blasenkatarrhs," First Congress of the German Gynæcological Society, Munich, 1886) first made use of Koch's plate cultures in making bacteriological examination of eight cases of cystitis occurring in puerperal

women. He found a diplococcus in all of the specimens examined, associated in some of them with the gonococcus or the staphylococcus pyogenes aureus. The microbes cultivated from the urine were also found in the lochia, which led him to conclude that the cystitis was caused by the use of the catheter. Cultures made from the urine injected into the bladders of dogs caused cystitis only in case the mucous membrane had been previously injured by retention of urine or the action of chemical irritants.

In 1887 Clado described a microbe which he found in the urine of patients suffering from cystitis, which he called "bactérie septique de la vessie." This microbe grew upon gelatin, which it liquefied, and rendered the nutrient medium alkaline. Pure cultures injected into the tissues of mice and rabbits produced septicæmia. Injections of the same into the bladder obstructed by ligature of the penis caused severe cystitis.

In 1889 Doyen described fourteen kinds of microbes in the urine of cystitis patients, ten kinds of bacilli, and four kinds of micrococci. Pure cultures of any of the bacilli injected into the peritoneal cavity of guinea-pigs was followed by death in from five to twenty-four hours. There is but little doubt that most of the bacilli found by French investigators in the urine of patients suffering from cystitis are identical with the colon bacillus.

In 1890 Lundström described two kinds of cystitis microbes, staphylococcus ureæ liquefaciens and staphylococcus ureæ candidus, both of which rendered the urine alkaline, besides causing the cystitis. Pure cultures injected into the bladders of rabbits, combined with temporary retention, caused cystitis of a suppurative type.

Albarran and Halle ("Note sur une bactérie pyogène et rôle dans l'infection urinaire," *Bulletin de l'Académie de Médecine*, August 21, 1888) were the first to make a systematic bacteriological investigation of the urine in cystitis. Their work is based on a study of fifty cases of suppurative cystitis, pyelonephritis, and kidney abscess. In forty-seven of these cases they found numerous bacilli; in fifteen of these, bacilli could be cultivated separately in pure cultures; in the rest cocci were also present. The bacillus was called "bactérie pyogène," and Albarran came to the conclusion, as the result of his investigations, that this organism produced the greatest number of cases of cystitis.

Melchior ("Om Cystitis og Urininfection kliniske eksperimen-



telle og bakteriologiske Studier," 1893) found the colon bacillus (*urobacillus communis*) in twenty-five out of thirty cases of cystitis, seventeen times as an isolated microbe. The bacterium next in frequency was the streptococcus pyogenes, which was found five times, three times in pure culture. In one case he cultivated from the urine the bacillus of typhoid fever, in a patient suffering from cystitis, two weeks after convalescence. From a scientific as well as from a practical stand-point it is time to admit that cystitis is invariably a microbial disease, and that the proper prophylactic precautions consist in preventing the entrance of microbes into the bladder, more especially in cases of urine retention and when the bladder is the seat of a lesion which offers a predisposition to infection. It is necessary to consider carefully and in detail the different avenues through which the bladder is reached by pathogenic microbes which are known to produce inflammation of this organ.

*Infection through the Urethra.*—Every surgeon is familiar with the frequency with which the passage of instruments into the bladder is followed by cystitis, particularly when the urethra is the seat of inflammation and in case catheterization is performed for retention of urine and the strictest aseptic precautions are not observed. By continuity of surface a suppurative inflammation of the urethra may extend to the bladder without instrumental intervention. Complete sterilization of catheter and hands does not always succeed in depriving catheterization of the danger of bladder infection. Pathogenic microbes are almost constantly found in the normal urethra of healthy persons.

Lustgarten and Mannaberg ("Ueber die Mikroorganismen der normalen männlichen Urethra," *Vierteljahrsschrift für Dermatologie und Syphilis*, 1887, p. 405) made a bacteriological examination of the urethras of eight healthy men, and found ten different kinds of microbes, among them many which are known to produce cystitis. These observations have been fully corroborated by the researches of Rovsing, Steinschneider and Galewsky, Legrain, Melchior and Petit, and Wassermann. The meatus is a favorite lodging-place for microbes. If the meatus is not disinfected before the insertion of the catheter, microbes may be carried with the instrument into the bladder sufficient in number and virulence to provoke a cystitis, provided they are brought in contact with a soil prepared for their reception and growth by an injury

or antecedent lesion. During a recent visit to the obstetrical wards of Professor von Winckel I was informed that for some time quite a large number of the recently delivered women had suffered from cystitis. The strictest antiseptic precautions were practised in sterilizing instruments and hands, but the prevalence of this puerperal complication continued until the professor introduced an additional precautionary measure, in all cases requiring the use of the catheter, —namely, disinfection of the meatus with a solution of the mercuric bichloride. From that time on cystitis from this cause disappeared. Secondary gonorrhœal cystitis following a specific urethritis, although a rare complication, does occur, but is more prone to follow a mixed infection of the urethra.

*Infection by the Urine.*—Authors continue to insist that practically the urine is sterile, and that infection of the bladder from this source seldom if ever occurs. This statement does not agree with accurate clinical observations or the results of examination of normal urine secreted by healthy kidneys. In some cases the passage of microbes through the kidneys produces temporary lesions which appear before the urine contains bacteria.

Schweiger ("Ueber das Durchgehen von Bacillen durch die Nieren," *Virchow's Archiv*, Band c., Heft 2) has shown conclusively by his careful clinical observations that the urine from scarlatinal patients is contagious; for varicella, typhus recurrens, and malaria the same holds true. In typhus, Gaffky has found bacilli in the renal vessels. As in most infective diseases the kidneys show textural changes; it is natural to conclude that the renal lesions were caused by microbes on their way out of the body. Schweiger looks upon all kidney lesions found in the course of infective diseases as of bacillary origin. To prove that microbes pass through the kidneys, he cultivated a bacillus which Reimann had discovered in the pus of ozæna. This bacillus is stained an intense green color in a culture of gelatin and agar after twenty-four hours. The cultures of this green bacillus were suspended in a sterilized physiological solution of salt, and injected directly into the circulation. The experiments were made on a dog, a cat, and a rabbit. The bacillus did not pass directly through the kidneys, but a certain length of time intervened between the injection and the appearance of the bacillus in the urine, as though somewhere an obstacle to the free passage had been met with. At first only isolated bacilli ap-



peared in the urine, but later they were found in large numbers. In one instance he extirpated one kidney, and two days later, during the first stage of compensatory hypertrophy of the remaining organ, he injected a culture directly into the carotid artery. The animal died suddenly, two and one-half hours after the injection, in an attack of convulsions. Under strict antiseptic precautions the urine was removed from the bladder, and with it a culture of agar-agar was inoculated. The next day the culture showed a beautiful growth of the same bacillus. The author believes that the kidney, the seat of increased vascular pressure, furnished a favorable condition for the rapid passage of the microbe. He found the microbes most frequently in the glomeruli and in the space between these and Bowman's capsule; and again, quite abundant in the blood-vessels and in the lumen of the first portion of the convoluted tubuli uriniferi, and only rarely in the perivascular spaces. Only once was a bacillus found between two epithelial cells of the convoluted tubules. In the cells themselves no bacilli were found.

Seitz found the bacillus of typhoid fever in the urine in two out of seven cases, Konjajeff in three out of twenty cases, Knepe once in sixteen cases, and Neumann in eight out of forty-eight cases. The last observer ("Ueber Typhus Bacillen im Urin," *Berliner klinische Wochenschrift*, February 10, 1890) in some instances found them so numerous that under the microscope the urine appeared like a fluid culture. In such cases the bacillus multiplies in the bladder. In two cases he also found the streptococcus pyogenes, an occurrence which he considered as an evidence of the existence of complications.

Sittmann (*Deutsches Archiv für klinische Medizin*, September 4, 1894) reports the results of experiments to determine the elimination of staphylococci with the urine. Rabbits were used in the experiments, and were injected in the vein of the ear with staphylococcus pyogenes aureus. After varying intervals the animals were slowly killed with chloroform and cultures made from the arterial and venous blood obtained from the right and left ventricle and from the urine. The microbes were invariably found in the urine. In the severe infection the bacteria appeared after eight hours, in lighter infection after five hours; and this condition was so constant that it was possible to predict the degree of virulence of the infection by the time of appearance of bacteria in the urine.

The elimination ceased, as a rule, after forty-six hours. The author makes the statement that staphylococci can be eliminated with the urine without causing serious damage to the kidney.

Neumann ("Ueber die diagnostische Bedeutung der bakteriologischen Untersuchungen bei inneren Krankheiten," *Berliner klinische Wochenschrift*, 1888, Nos. 7, 8, and 9) found the specific microbes in the urine in cases of typhoid, septicæmia, and pyæmia. In a case of acute endocarditis and acute osteomyelitis, he cultivated from the urine the staphylococcus pyogenes aureus. He believes that the micro-organisms which circulate in the blood localize in the capillary vessels of the kidney, where they often cause minute multiple lesions without implication of the entire parenchyma of the organ. Through the altered tissues some of the microbes enter the tubuli uriniferi and are eliminated with the urine.

The elimination of tubercle bacilli with the urine in phthysical subjects and in animals rendered tubercular by inhalation or inoculation has been proved by many reliable clinical observers and careful experimenters.

Philipowicz ("Ueber das Aufbreiten pathogener Microorganismen im Harne," *Wiener medicinische Blätter*, 1885, No. 22) found the bacillus of tuberculosis in the urine not only in three cases of tubercular pyelonephritis, but also in cases of acute miliary tuberculosis. If the organisms were not present in sufficient number for detection by the microscope, their presence in the urine could be proved by the injection of the urine into the peritoneal cavity of guinea-pigs. He also found bacilli in the urine in cases of glanders. In mice which had died of anthrax the urine contained bacilli in large numbers. In patients who had succumbed to ulcerative endocarditis, pus microbes were found in the urine.

Lentz ("Experimentelle Untersuchungen über die Infektiosität des Blutes und Urines Tuberculöser," Dissertation, Greifswald, 1881) demonstrated the infectiousness of the urine of tubercular persons by inhalation experiments on five rabbits. The animals were confined in a box into which the steam of an atomizer mixed with the urine of two phthysical patients was introduced. For each two of the animals at one sitting thirty to forty cubic centimetres of urine were vaporized. In two of the animals the experiment was continued daily for seventy-one consecutive days. The animals were then killed, and numerous tubercles were found in the lungs,



peribronchial glands, and liver. In three of the animals the urine was allowed to decompose under a cover of filter-paper, when it was administered by the same method. One of the animals died in consequence of an abortion on the ninth day, one was killed on the forty-eighth day, the other on the sixty-ninth day. In all of the animals well-marked tubercular processes were found in the lungs and bronchial glands. The inhalation of urine from healthy persons proved harmless. From the clinical experience and the results of experimentation quoted it is evident that the elimination of pathogenic microbes through healthy kidneys may become a source of bacterial invasion of the bladder sufficient in intensity to produce an inflammation if the microbes find a soil favorable for their reception and growth. This route of infection must be suspected in all cases of cystitis in which more direct infection and infection from the blood can be excluded. The existence of a suppurative affection of the kidneys or pelves, which so often precedes a similar disease of the bladder, greatly enhances the danger of infection by the urine, as the pus microbes multiply in the suppurating focus or foci and reach the bladder by way of the urine in immense numbers, besides the tendency of the infective process to extend from the primary lesion along the ureters to the bladder by continuity of surface.

*Infection from Adjacent Organs.*—The bladder is often involved secondarily by the direct or indirect extension of an infective process from one of the adjacent organs. In females cystitis secondary to suppurative affections of any of the pelvic organs is of frequent occurrence. The bladder may become involved by the direct extension of an infection from its vicinity, or by infection through the lymphatics. In the latter case the inflammation is first interstitial, but may involve the mucous lining by extension of the infective process or by the rupture of an interstitial abscess into the bladder. Extension of a suppurative process in the region of the appendix or the prevesical space in the direction of the bladder is also not infrequently the direct cause of a suppurative cystitis. From an etiological stand-point cystitis caused by the migration of microbes from the intestinal canal is of the greatest importance, and has recently excited a wide-spread interest among bacteriologists and surgeons. The microbe which finds entrance most frequently into the bladder by this route is the bacillus coli commune. The

lymphatics are undoubtedly the channels through which the invasion takes place. This microbe is found so constantly in the intestinal canal, even in healthy persons, and is, according to recent researches, so often found as the sole microbic cause of cystitis, that we are forced to admit that this mode of infection is of frequent occurrence. Clinical data as well as the results of experimentation combined to prove that the bladder is most frequently infected with this microbe from the rectum. The migration of the colon bacillus from the intestinal canal into the bladder under certain conditions has been assumed by Fränkel, Tavel and Lanz, Arnd, Ziegler, and Blom.

Posner and Lewin ("Untersuchungen über die Infektion der Harnwege," *Centralblatt für die Krankheiten der Harn- und Sexual-Organe*, 1896, Band vii., Heft 7 and 8) have furnished experimental proof of the possibility of such an occurrence. Their experiments on animals consisted in first making an intestinal obstruction by closing the anal orifice either by ligature or clamp. After one or two days the urethra was made impermeable in a similar manner. A day or two later the animal was killed and the urine examined. In a number of successful experiments a pure culture of the colon bacillus was found in the urine. These experiments prove that infection of the bladder from the rectum may take place without any gross intestinal lesions. In the same manner colored solutions injected into the rectum found their way into the bladder. Experiments with the bacillus prodigiosus and pyocyaneus yielded the same results. These observers found as the microbic cause of cystitis the bacillus coli, proteus vulgaris, staphylococcus pyogenes aureus and albus, and several times diplococci.

Wreden (*Blätter für klinische Hydrotherapie und verwandte Heilmethoden*, 1895, No. 5), in his experiments on rabbits made for the purpose of demonstrating the possibility of infection of the bladder from the rectum, assured himself first that the urine was free of micro-organisms, then he injured the rectal mucous membrane by injections of very hot water, croton oil, or by irritating it by mechanical means, with the result that cystitis developed, and examination of the urine showed the existence of the same microbes as were found in the rectum. If a tampon containing the proteus or the bacillus mesentericus vulgaris was introduced into the rectum

prepared for infection in a similar manner, the bacilli sooner or later appeared in the bladder.

R. Fultin ("Beiträge zur Frage von den Wegen auf denen *Bacterium coli communis* in die Blase eindringt," Dissertation, Helsingfors, 1896) repeated the experiments of Wreden, and never observed bacteriæmia. In experiments in which the kidneys were damaged by cantharidin the bacillus coli injected directly into veins appeared in the urine. In one series of experiments he injured the rectal mucous membrane with a sharp curette or croton oil, or both, after which carmine-stained bacteria were injected into the rectum. No cystitis resulted and no bacteria could be found in the bladder. In another series of experiments the rectum was treated in the same manner before injecting the microbes, after which the penis was ligated for from twenty-four to twenty-eight hours. In nearly all of these cases the microbes found their way into the bladder in sufficient quantity and virulence to produce cystitis in from three to four days. In a third set of experiments only the penis was ligated. After the removal of the ligature bacteriæmia was found in about one out of five cases. If the animal were catheterized before ligation of the penis, or if the ligature were renewed after two or three days, a cystitis developed almost invariably. In the last experiments the rectum was seriously injured before the bacterial injection was made. In some of the experiments bacteria entered the bladder and produced cystitis, but peritonitis was also observed with about the same degree of frequency. In these cases bacteria were also found in the blood and kidneys. If the animals survived, the urine remained sterile, except in one instance, in which a cystitis developed slowly after a few days. In drawing conclusions from the results of his experiments, he admits that in some instances the bladder may become infected from the rectum, but he maintains that this mode of infection is comparatively rare and not as constant as claimed by Wreden. Clinical observations fully corroborate what has been established by experiments on animals,—namely, that cystitis is quite frequently caused by infection from the rectum, and that this method of infection is very likely to take place when lesions of the mucous membrane of the rectum are present, which admit of a more ready entrance into the tissues and migration of the bacillus coli, and when the bladder, from retention of urine or



antecedent injury or disease, is in a condition of increased susceptibility to infection.

*Infection from the Blood.*—In rare cases infection of the bladder takes place by microbes which float in the general circulation with or without an antecedent or coexisting suppurating depôt in some other part of the body. It has become an established fact, in connection with the origin of many of the surgical infective lesions, that the blood in the general circulation contains pathogenic microbes which produce no ill results until some tissue or part of the body becomes prepared for their localization and growth, when infection takes place in the prepared soil. Such direct connection between cause and effect has been repeatedly demonstrated experimentally between pyogenic microbes in the general circulation and the causation of suppurative osteomyelitis, synovitis, peritonitis, and tuberculosis of bones and joints. It is only rational to assume that in rare cases cystitis is produced by this method of invasion. We should naturally expect that in such cases the infection begins beneath the mucous membrane or in the middle coat, and that the lesion of the mucous membrane resulting as a secondary consequence begins as a circumscribed affection and often remains so unless retention of urine sets in and favors the dissemination of the infection over the surface of the mucous lining of the bladder. Ulcerative cystitis unquestionably has occasionally such an origin. In other cases pyogenic microbes are eliminated in sufficient number through the intact kidneys and reach the bladder with the urine, retaining a sufficient degree of virulence, when brought in contact with a favorable soil, to induce an attack of cystitis. Usually under such circumstances the cystitis is of a diffuse character. Retention of urine in such instances constitutes the most frequent predisposing cause. Infection from the blood in the causation of cystitis merits further experimental study, which will undoubtedly throw more important light upon the etiology of this disease. In recapitulating what is known of the causes of cystitis, I am warranted in stating that a healthy bladder containing normal urine is seldom attacked by inflammation, and that when inflammation of this organ does occur, it is in consequence of the presence of one or more of the predisposing causes which have been enumerated and the entrance into the bladder through one of the routes mentioned of pathogenic microbes in sufficient number and virulence to produce inflamma-

tion in the tissues prepared for their pathogenic action by antecedent or co-existing injuries or disease.

## II. CLASSIFICATION OF CYSTITIS.

A rational classification of cystitis is essential in discussing the etiology, symptomatology, diagnosis, prognosis, and treatment of this disease. The surgeon is no longer content to simply recognize the existence of the disease. To enable him to estimate the gravity of the affection and to adopt an intelligent course of treatment, he must be in possession of an accurate knowledge of its real nature, location, and extent. He must know what microbe or microbes have produced the inflammation before he can make a diagnosis that will suggest the necessary therapeutic indications. Mistaken and inaccurate diagnoses are largely responsible for the many short-comings of our present therapeutic resources. For the purpose of showing some of the defects of the methods of classification of cystitis heretofore made by authors who have made a special study of this disease, I will give only the classification made by Guyon and Rovsing.

*Guyon's Classification of Cystitis.*—1, Cystite blennorrhagique; 2, cystite tuberculeuse; 3, cystite calculeuse; 4, cystite des rétreicis; 5, cystite des prostatiques; 6, cystite des néoplasiques; 7, cystite chez la femme; 8, cystite douloureuse; 9, cystite membraneuse.

I can see no reason for discussing cystitis as it occurs in women as a separate affection; neither is it necessary in classifying cystitis to consider separately the different causes which give rise to irritation of the bladder or retention of urine. Cystitis is always a painful affection, and there is absolutely no excuse for setting aside a class of cases in which this symptom may be more prominent than in others as a separate variety under the head of cystitis douloureuse.

*Rovsing's Classification of Cystitis.*—1, Cystitis catarrhalis; 2, cystitis suppurativa. The latter class he subdivides again into (a) cystitis suppurativa ammoniacalis and (b) cystitis suppurativa acidula. s. tuberculosa.

Rovsing's classification has special reference to the action of the essential microbic cause on the urine and the tissues of the bladder, but it is well known that in many cases of non-tubercular cystitis the urine is acid, especially in cases in which the colon bacillus is found as the sole microbic cause. This classification also ignores

almost completely the different pathological varieties with which the surgeon must be familiar in order to comprehend the nature and extent of the disease. No classification is complete which does not indicate the anatomical location, the clinical features, pathological characteristics, and bacteriological origin of the disease.

1. *Anatomical Classification*.—(a) Pericystitis; (b) paracystitis; (c) interstitial cystitis; (d) endocystitis.

(a) *Pericystitis*.—Cystitis is the term usually employed in designating an inflammation of the bladder without any special reference to what tissues are the seat of the inflammatory process. In the diagnosis of all diseases it is of the greatest importance to determine, if possible, the organ or tissues in which the disease had its starting-point; in other words, to make first an anatomical diagnosis. Although the mucous membrane of the bladder is most frequently primarily affected in cystitis, either of the remaining two tunics may be the primary starting-point of the inflammatory process from which the infection may or may not extend to the mucous membrane, but the symptoms usually point in that direction.

Guyon ("Diagnostic différentiel de certaines formes de la cystite et des néoplasmes de la vessie," *Annales des Maladies des Organes Génito-urinaires*, 1895, No. 4) calls attention to the great difficulties which the surgeon frequently encounters in the differential diagnosis between cystitis and neoplasms of the bladder. He demonstrated in his clinic two patients in which, besides the usual symptoms of cystitis, an infiltration of the bladder wall simulated tumor. Suprapubic incision of the bladder cleared up the diagnosis, as it revealed a well-marked pericystitic infiltration. In a third case the symptoms which had existed for eight months appeared to point directly to cystitis, when a perineal section made it clear that it was a case of carcinoma.

In pericystitis the peritoneal coat of the bladder is the seat of inflammation; it is in reality a vesical peritonitis. This anatomical form of cystitis follows usually in consequence of the extension of an inflammation from one of the adjacent organs,—the appendix, uterus, tubes, or ovaries; in rare instances it is caused by intestinal perforation. The inflammatory product is most abundant around the base and at the sides of the bladder. At the sides of the bladder, at a point corresponding with the vesical end of the ureter, the inflammatory masses often reach considerable size, and by cicatricial



contraction may eventually cause ureteral obstruction. In the female, vesical peritonitis is usually secondary to pelvic peritonitis. The immobilization of the bladder by adhesions and the vascular disturbances caused by the pericystitis are often productive of great vesical distress, and secondary pathological changes often reach the mucous membrane of the bladder.

Dacheux (*Centralblatt für Gynäkologie*, 1895, No. 40) believes that the condition of irritable bladder in women, which has previously been regarded as a purely functional disorder, is really, as Zuckerkandl states, due to localized hyperæmia of the mucous membrane, which can be demonstrated by cystoscopic examination. Hyperæmic patches are seen at the base of the bladder, and less often at the neck, which bear a close etiological relation to concomitant congestion of the uterus and adnexa, and often disappear when the latter is relieved.

Kolischer (*Centralblatt für Gynäkologie*, 1895, No. 27) describes, in connection with such cases, a peculiar form of oedema of the mucous membrane of the bladder observed through the cystoscope. It appears in the form of circumscribed blisters the size of a pea, the rest of the membrane being normal. In some cases the blebs are so large as to resemble vesicular moles. This pathological condition is always associated with pelvic exudates near the bladder, and is seen most frequently in women the subjects of salpingitis. The symptoms which attend this form of vesical irritation are painful urination, tenesmus, and a feeling of weight and pressure over the bladder. While the clinical symptoms indicate the presence of cystitis, examination of the urine yields negative results, unless the infection has extended to the mucous membrane of the bladder.

(b) *Paracystitis*.—Paracystitis is an inflammation of the subperitoneal connective tissue of the bladder or of the surrounding connective tissue where the bladder is extraperitoneal in the cavum Retzii and prostatic portion of the organ. At the base of the bladder a paracystitis not infrequently develops in the course of a suppurative prostatitis, and in front of the bladder the disease usually appears in the form of a phlegmonous inflammation of the loose connective tissue in the cavity of Retzius. In both of these locations abscess formation is the usual termination of the inflammatory process, an occurrence always attended by distressing bladder symptoms. Abscesses in both of these places, unless incised early, are

very prone to rupture into the bladder, an accident which is often followed by an obstinate cystitis. Inflammation of the subserous connective tissue, following infection through the lymphatic channels, is a very obscure affection, and a positive diagnosis is more frequently made in the post-mortem room than at the bedside. The formation of multiple abscesses in such cases is not an unusual occurrence. More or less pericystitis is almost always associated with pericystitis involving the intraperitoneal portion of the bladder.

(c) *Interstitial Cystitis*.—Interstitial cystitis implicates the middle tunic or muscular coat of the bladder. It is in this coat that we find the lymph channels most numerous and consequently the most common pathways of infection. Invasion of the middle coat may take place from either direction, either by extension of infection from the mucous lining, or the microbes may reach the muscular coat through the lymph-channels from some adjacent inflammatory focus. Another, but perhaps the rarest, route of infection is through the circulation, when the interstitial cystitis is initiated by an endo- or perivascular inflammation. Direct extension of inflammation of the mucous membrane to the muscular coat, or invasion by way of the lymphatic channels, usually leads to a diffuse inflammation in which the whole middle coat may participate, in which case it becomes greatly thickened and the mucous membrane is changed into folds. Ridges can be felt with the sound. Interstitial cystitis usually leads to abscess formation. Small abscesses develop in the submucous connective tissue, or in the muscular coat, which, when they open into the bladder, leave diverticula which heal slowly and in which calculi are often found concealed. Recovery from this form of cystitis often results in a great diminution in the size of the bladder, caused by cicatricial contraction. In the embolic form of interstitial cystitis circumscribed inflammation and abscess formation are the usual results of the infection.

(d) *Endocystitis*.—What is ordinarily understood by cystitis is an inflammation of the lining membrane of the bladder. The inflammation may almost from the beginning, or at any rate in a few days, involve the entire surface of the mucous membrane, or it may remain limited to certain localities which are most exposed to infection. Localized cystitis is found most frequently in the trigonum and about the urethral and ureteral orifices; it is also from these points that diffuse cystitis has its starting-point. The neck

of the bladder is the most sensitive part of the organ, and it is here that inflammation gives rise to the most distressing symptoms. In cystitis proper the urine contains, almost from the very beginning, the morphological elements of the inflammatory product,—blood, epithelial cells, and pus-corpuscles,—the presence of which always constitutes an important distinguishing feature between endocystitis and the other anatomical varieties of inflammation of the bladder. In the further discussion of the classification of cystitis, endocystitis, or cystitis proper, will be taken as the type of the disease.

2. *Pathological Classification.*—(a) Catarrhal cystitis; (b) suppurative cystitis; (c) ulcerative cystitis; (d) exudative cystitis; (e) exfoliative cystitis.

The effects of microbes and their toxins on the tissues of the bladder vary according to the specific pathogenic effect of the original bacterial cause and the number of microbes and their degree of virulence. The inflammatory product is also greatly influenced by the condition of the urine and the nature and extent of the predisposing causes. The successful treatment of cystitis is often materially influenced by the character of the inflammation and the nature of complications which may precede, attend, or follow cystitis. I am sure every surgeon will appreciate the value and importance of a clear pathological classification of cystitis for the purpose of grouping his cases properly from a pathological standpoint and as a reliable aid to diagnosis and treatment. The pathological classification must be based entirely on the character of the inflammatory product.

(a) *Catarrhal Cystitis.*—For a long time catarrh of the bladder has been regarded as synonymous with chronic inflammation. German writers have been particularly partial to this term, which has made so much confusion in the literature on inflammatory affections of the bladder. From a modern pathological standpoint catarrhal cystitis is a term used to indicate the existence of a superficial inflammation of the interior of the bladder in which the epithelial cells furnish the principal part of the morphological elements of the inflammatory product. It is, like all catarrhal inflammations in other localities, a surface affection. The mucous membrane is swollen, red, and the inflammatory process consists in increased exfoliation of epithelial cells and an abundance of mucus formation. If the disease becomes chronic, thickening of the mucous membrane



and secondary infiltration of the muscular coat lead to hypertrophy of the bladder wall. Retention of urine aggravates the inflammation and increases the vesical distress. Erosions and superficial ulcerations may develop during the course of the disease. The urine is usually acid, and contains pus and an abundance of bladder epithelium. In cases in which the urine has undergone alkaline decomposition the inflamed surface presents a dirty-whitish deposit of muco-pus.

Rovsing ("Om Blaerebetaendelsernes Aetiologi, Pathogenese og Behandling," Kjoebenhavn, 1889) is of the opinion that in catarrhal cystitis the microbes which produced the disease do not attack the mucous membrane of the bladder, but that they provoke the disease by rendering the urine ammoniacal, while in suppurative cystitis, in addition to this, their pyogenic action is expended upon the mucous membrane prepared for their specific action on the tissues by the preceding catarrhal inflammation. It is not always easy and sometimes impossible to draw a sharp line between catarrhal cystitis and suppurative cystitis because the latter frequently follows upon the footsteps of the former, and the transition is often so gradual that it is impossible to tell where one ends and the other begins. From a clinical stand-point the differentiation between these closely allied inflammatory affections of the bladder is perhaps attended by less difficulty, as suppurative cystitis gives rise to more serious constitutional disturbances than catarrhal cystitis, owing to the existence of a more intense infection and more extensive involvement and destruction of tissue.

(b) *Suppurative Cystitis*.—Suppurative cystitis appears clinically usually as a diffuse affection, in which not only the epithelial lining but also the deeper structures are generally involved. The microbial infection is of sufficient intensity to destroy the protoplasm of the morphological products of the inflammation, white corpuscles purely epithelial, and connective-tissue cells, and transform them into pus-corpuscles. The urine contains large quantities of pus and bladder epithelium. During the acute stage small fibrinous patches appear upon the inflamed surface. Ulceration differing in extent and depth is of common occurrence. Deep necrosis may lead to perforation. If the urine is ammoniacal, the necrosed patches present a grayish-white color and are encrusted with sand-like deposits. The decomposition of the urine is generally due to other microbes

than those which have caused the suppurative inflammation; that is, it is generally the result of a mixed infection. Besides the usual pyogenic microbes, the ammoniacal urine contains some species of saprophytic bacteria or the diplococcus ureæ. Suppurative cystitis generally begins as an acute inflammation, but is very liable to pass into the chronic form, and direct extension of the infective process is liable, sooner or later, to implicate the kidneys.

(c) *Ulcerative Cystitis*.—In this class of cystitis it is not my intention to include the cases of suppurative cystitis which terminate in ulceration which would only indicate an advanced stage of the disease, but I desire to limit the application of the qualifying term ulcerative to a form of cystitis in which ulceration takes place almost from the beginning of the inflammation. In cases of this kind the infection appears to be of a peculiar kind, limited in extent, and the resulting inflammation leads quickly to a circumscribed destruction of tissue, the formation usually of a single circumscribed ulcer, the so-called “simple” ulcer of the bladder. This form of cystitis is quite rare, and resembles in many respects gastric ulcer and the round duodenal ulcer.

Fenwick (*British Medical Journal*, May 9, 1896) has seen a number of cases of simple, solitary ulcer of the bladder. The disease is usually met with in young men without a venereal history. The first symptom is increased desire to urinate, coming on suddenly; intermittent hæmaturia then appears. He describes three stages. In the first stage the urine is acid, the specific gravity high, and pus scanty. In the second stage the ulcer becomes encrusted with phosphates, and fragments of the deposit break off now and then and are passed with painful paroxysms, or are retained and serve as nuclei for calculus formation. During the third stage the bladder becomes contracted, the mucous membrane extensively ulcerated, and ureteral and renal lesions arise. Solitary ulcer is clinically indicated if the urine is clear and normal in specific gravity and reaction, and if there is constant penile pain and absence of nocturnal irritability. This form of cystitis is undoubtedly the result of an infection from the blood, the inflammation attacking the tissues around an infected embolic infarct, reaching the surface of the bladder by a process of ulceration. Like gastric and duodenal ulcer, ulcerative cystitis is found, as a rule, in young adults,

and usually without any antecedent or attending predisposing local causes.

(d) *Exudative Cystitis*.—Inflammation of the mucous membrane of the bladder accompanied by the deposition upon the inflamed surface of the products of coagulation necrosis should be called exudative cystitis. The descriptive terms, membranous, diphtheritic, croupous, and fibrinous, are confusing and misleading and should be excluded from the present nomenclature in the description of this pathological form of cystitis. The exudate consists largely of fibrin, and is variously modified in quantity and appearance by the character of the infection and the condition of the urine. The exudate is the best possible proof of the severity of the infection and intensity of the inflammation. It proves the existence of a deep-seated lesion and great damage to the blood-vessels in the inflamed tissues. This form of cystitis is most frequently observed in puerperal women and women suffering from pelvic tumors large enough to subject the bladder to harmful pressure.

According to Stein, of fifty cases of exudative cystitis, forty-five occurred in women mostly in connection with the puerperal state or tumors of the uterus. In the milder types of this disease the mucous membrane under the fibrinous exudate is vascular and swollen; in the grave cases the mucous membrane and submucous connective tissue are often extensively destroyed by acute necrosis or ulceration.

Adami (*Montreal Medical Journal*, July, 1894) studied a case of this kind in a woman the subject of a myofibroma of the uterus large enough to produce considerable pelvic pressure. To pressure and obstruction of the lymph-stream he attributed important elements in the etiology of this variety of cystitis. The membranes and shreds were passed after great pain and distress. The membranes were found to be composed of a large amount of fibrin, and incorporated in this what were evidently layers of the bladder wall. In many of the cases not only epithelial layers but a certain amount of the muscle tissue of the bladder wall has thus become destroyed.

Savor ("Cystitis crouposa bei saurem Harn," *Wiener klinische Wochenschrift*, 1895, No. 44) observed a case of exudative cystitis on the fourth day after extirpation of the uterus by the abdominal route. Catheter was not used either before or after operation. Membranes five to ten centimetres in length were expelled with the urine. These membranes were composed of fibrin and contained in



the meshes of the fibrin numerous pus-corpuscles. The urine was ammoniacal only for one day. In the urine sediment the colon bacillus was found, and was regarded by the author as the essential microbic cause of the inflammation. Savor made experiments with pure cultures of this bacillus with a view of reproducing this special form of inflammation upon serous and mucous surfaces of other organs in animals, but the results of his endeavors proved negative. The urine in exudative cystitis is usually alkaline, and Savor believed that in his case it remained acid after the first days owing to the absence of a mixed infection. In the majority of cases exudative cystitis occurs in women during the childbearing period and positive proof of the pathological nature of the cystitis is always furnished by the expulsion of membranes or shreds of fibrin with the urine.

(e) *Exfoliative Cystitis*.—Exfoliative cystitis is an inflammation of the bladder in which, almost from the very beginning, the toxins of the microbes which produced the disease destroy the mucous membrane and sometimes even the muscular coat, which, if the patient survive, become detached with the inflammatory product and are expelled with the urine, or in some instances have to be extracted from the bladder by the surgeon. This is the most dangerous form of cystitis, and can only occur as the result of a most virulent infection, aided in most cases by local predisposing causes. In exudative cystitis the toxins precipitate the inflammatory product by causing coagulation necrosis; in exfoliative cystitis they cause necrosis of the mucous lining of the bladder and occasionally also of the muscular coat. The same mechanical causes which are so influential in causing exudative cystitis are usually present and active in the production of exfoliative cystitis. In a few cases carcinoma of the bladder appears to have been the predisposing cause of this form of cystitis, with the result that the disease was completely removed by the extensive sloughing, and in a few instances the patients not only recovered from the cystitis, but were permanently cured of the carcinoma by the complete elimination of the malignant tissues with the product of the exfoliative process.

A very interesting case of extensive exfoliative cystitis is reported by J. C. Warren (*Boston Medical and Surgical Journal*, June 25, 1896). Under an anæsthetic "rolls of sloughing tissue" were extracted with forceps until a "membrane the size of a small pocket-handkerchief" had been removed from the bladder in a con-

nected mass. The patient suffered first from incontinence, but gradually recovered under daily washings out of the bladder with a weak solution of potassium permanganate, and later with a solution of boracic acid. An examination of the specimen removed showed it to be of a character similar to the submucosa of the bladder.

Boldt (*American Journal of Obstetrics*, April 27, 1889), under the term suppurative exfoliative cystitis, describes this form of cystitis, marked by inflammatory separation *en masse* of portions of the mucous lining of the bladder, due especially, as he believes, to posterior displacements of the gravid uterus, to undue or prolonged pressure of the foetal head in labor, or to other mechanical causes. The degree and extent of the exfoliation vary with the intensity of the mechanical cause and the virulence of the infection. The differentiation between exudative and exfoliative cystitis can only be made by a careful study of the membranes, shreds, or masses expelled or removed from the bladder, which often must necessarily include the use of the microscope as a diagnostic aid.

3. *Clinical Classification*.—(a) Acute cystitis; (b) chronic cystitis.

(a) *Acute Cystitis*.—The old and usual clinical diagnosis is based on the intensity of symptoms and duration of the disease. That form of inflammation of the bladder in which the symptoms appear suddenly and reach their maximum height in a short time is known as acute cystitis. In this class of cases the infection is intense, the constitutional disturbances well-marked, and the nature of the pathological products in accordance with the acuity of the inflammatory process. One of the best illustrations of what is meant by acute cystitis is furnished by cases of urine retention in which infection occurs by the use of the catheter. The disease is usually initiated by a chill followed by febrile reaction; the urine becomes turbid within twenty-four hours, and in a few days contains large quantities of pus, and ammoniacal decomposition is developed very rapidly. It is not difficult in the majority of cases to establish the existence of acute cystitis, but such a diagnosis no longer satisfies the surgeon who seeks to complete his diagnostic work by investigating the pathological anatomy of the disease and by ascertaining the nature of the infection. Under appropriate treatment an acute cystitis may be under control in a short time, but in the presence of obstructive or visceral lesions the acute symptoms subside in the

course of time, when the disease only too often passes into the chronic form.

(b) *Chronic Cystitis*.—Chronic inflammation of the bladder is characterized by the absence of acute symptoms, local and general, and the tendency of the disease to persist regardless of the treatment employed. The suppurative form of chronic cystitis is usually complicated by the coexistence of stricture of the urethra, enlarged prostate, or the presence of stone or foreign body in the bladder. Cystitis caused by infection from a suppurative affection of the kidneys is also very prone to pursue a chronic course, as the constant irrigation of the bladder with infected pus maintains an uninterrupted source of infection. The best example illustrating the clinical aspects of chronic cystitis is furnished by the tubercular variety. The disease begins insidiously by the appearance of isolated symptoms which point to the bladder as the probable seat of the inflammation. The symptoms gradually increase in number and intensity until the complexus is complete upon which to base a diagnosis of chronic cystitis. The symptoms are often masked by complications which served as predisposing causes or which ensued in consequence of the chronic inflammation. It is in cases of chronic cystitis that an early and correct diagnosis is so seldom made. Renal disease is often mistaken for cystitis, and cystitis for renal disease. It is in such cases that a recourse to all modern diagnostic aids is indispensable for a correct interpretation of the symptoms as they arise. It is not unusual that patients suffering from incipient tuberculosis of the bladder go from one physician to another, and are repeatedly sounded for stone in the bladder, when perhaps the results obtained from a careful examination of the external genitals and the prostate would at once arouse suspicions in reference to the probable tubercular nature of the vesical affection. It is well to remember that in the majority of cases of chronic inflammation of the bladder not complicated by obstructive lesions the disease is of a tubercular nature.

4. *Bacteriological Classification*.—(a) *Bacillus coli commune* infection; (b) saprophytic (mixed) infection; (c) *staphylococcus* infection; (d) *streptococcus* infection; (e) *streptococcus erysipclatis* infection; (f) typhoid bacillus infection; (g) *diplobacillus* infection; (h) *gonococcus* infection; (i) bacillus of tuberculosis infection.

The bacteriological classification of cystitis is the most modern



and certainly the most important. The bacteriological classification has a direct bearing on the etiology of the disease, and suggests to the surgeon the most rational course to pursue in its treatment. In long-standing and obscure cases of inflammation of the bladder examination is not complete without an examination of the urine with sufficient care and thoroughness upon which to base a correct bacteriological classification. Surgeons must learn to appreciate the value and importance of this part of the examination before we can expect material advances in the treatment of cystitis. If the surgeon has not the necessary knowledge or equipment to make these examinations satisfactorily, he should assign this part of his task to a competent bacteriologist.

(a) *Bacillus Coli Commune*.—Bacteriological researches made by numerous observers go to prove that the bacillus coli commune is found more frequently in the urine of patients suffering from cystitis than any other known microbe, and all combine in assigning to it a more or less important rôle in the causation of the disease. This micro-organism was discovered by Escherich in 1886 ("Die Darmbakterien des Säuglings," Stuttgart, 1886). It is constantly found in the contents of the normal intestinal canal. Its presence in suppurative affections in different parts of the body has been repeatedly demonstrated, and its pathogenic qualities have been carefully determined. Since 1891 the colon bacillus has been demonstrated in the urine in cystitis patients by Achard and Renault, Reblaub, Haushalter, Hartmann, Guinon, and Denys, all of whom claim for it distinct etiologic qualities.

Rovsing ("Die Bedeutung des Bacterium Coli für die Pathologie der Harnorgane," Hospitals Tidende, No. 32, 1895) has reported a number of cases of infection of the upper portion of the urinary tract in which myriads of the colon bacillus were found in the urine without having produced cystitis. If in such cases another microbe finds its way into the bladder which will decompose the urine, cystitis invariably follows. The colon bacillus does not decompose urea. The ordinary pus microbes decompose the urine, and are almost constantly found in cases of cystitis in which the colon bacillus is found in abundance. The microbes which are known to decompose urea are bacterium pyocyaneus, cocci bacillus pyogenes ureæ, staphylococcus, and a special form of streptococcus found in decomposed urine.

Rovsing ascertained, also, that in dead culture media the colon bacillus exerts a destructive, or at least an inhibiting effect on the bacteria which decompose urine. The correctness of these observations is sustained by the investigations of Beco, Wothelet, Charin and Veillon, Tavel and Lanz, Albarran, Halle, Melchior, Guyon, Schmidt, Krogius, and Schoff, all assigning to the bacillus coli distinct and important pathogenic properties in the genesis of cystitis. Recent observations tend to prove that the colon bacillus requires the co-operation of urine-decomposing bacteria in the production of cystitis.

Trumpp ("Ueber Colicystitis in Kindesalter," *Münchener medicinische Wochenschrift*, 1896, No. 42) made a bacteriological examination of the urine in twenty-nine cases of cystitis in children (eight boys, twenty-one girls), in the clinic of Escherich. Of these cases, seventeen were suffering at the same time from follicular enteritis. In fourteen the bacillus coli was found. The cystitis in these cases was characterized by grave general symptoms, slow progression of the infective process in the direction of the kidneys, and occasionally a fatal nephritis.

Melchior found the urine acid in all cases of cystitis in which the colon bacillus was found as a solitary microbe. His experiments on rabbits, guinea-pigs, and mice with pure cultures injected into veins, beneath the skin, and into serous cavities proved the pyogenic properties of this microbe. He is of the opinion that many of the bacilli discovered in the urine of cystitis patients and described under different names are identical with the colon bacillus. Of thirty-seven cases of cystitis examined by Melchior, the colon bacillus was found in thirteen (twelve times solitary); diplococcus ureæ liquefaciens, eleven times (nine times solitary); proteus Hauser, five times (three times solitary); and staphylococcus pyogenes, four times (three times solitary). It seems that the colon bacillus under certain favorable circumstances can and does produce cystitis, but it is equally certain that its pathogenic properties are greatly enhanced when it is associated with bacteria which decompose the urine. It is found most frequently in the urine in cases of cystitis caused by a mixed infection. Colon bacillus infection should be suspected in all cases of cystitis following operations upon the rectum, and when the disease has followed or is coexistent with intestinal fermentation, irritation, or inflammation; also in cases in which the urine remains acid.

(b) *Saprophytic (Mixed) Infection*.—In more than one-half of all cases of acute and chronic cystitis, infection is the result of the presence and combined action of several different kinds of microbes. Pus microbes and the saphrophytes decompose the urine, rendering it alkaline. Ammoniacal urine acts as an irritant to the mucous membrane of the bladder, producing textural changes which prepare the way for the action of the bacteria, which are more directly concerned in the production of the inflammation. A mixed infection must be suspected in all cases in which the urine is ammoniacal.

Mesnil de Rochemont (*op. cit.*) cultivated from the urine of twenty-five cases of cystitis fourteen different kinds of microbes, one-half of which decomposed urea; the remaining half had no such effect.

Kastalskaya (*Zeitschrift für Geburtshülfe und Gynäkologie*, Band xxxv., Heft 1), from a bacteriological study of urine from the bladder in twelve cases of cystitis, reports the following results: In one case he found the bacillus *fœtidus liquefaciens* mixed with tubercle bacilli and non-pathogenic cocci; in five cases tubercle bacilli, twice as a pure culture, once mixed with non-pathogenic cocci and bacillus coli, and once with non-pathogenic cocci and the bacillus *fœtidus liquefaciens*; in four cases the bacillus coli, twice as a pure culture, once with non-pathogenic cocci and tubercle bacilli, and once with streptococcus pyogenes; in one case pseudobacillus coli commune as a pure culture; in one case bacilli with non-pathogenic cocci; in one case streptococcus pyogenes with bacillus coli; and in one case a pure culture of pseudostaphylococcus albus.

Lépine and Roux, of Lyons (*Comptes-rendus hebdomadaire des Séances de l'Académie des Sciences*, Paris, July, 1894) proved by numerous experiments with dogs and guinea-pigs that the introduction into the urethra of a pure culture of the micrococcus ureæ, followed by temporary ligation of the urethra, invariably resulted in ammoniacal fermentation of the urine and cystitis with grave lesions. Decomposition of the urine occasionally is attended by gas formation (pneumaturia), and in such instances some form of gasogenic bacteria can be found. Heyse (*Zeitschrift für klinische Medicin*, Band xxiv.) records a case of gas formation in the bladder of a patient suffering from myelitis with retention of urine. After catheterization had been practised for some time gas was noticed escaping through the catheter. Autopsy showed gas in considerable



quantities in the bladder, ureter, and substance of the kidneys. Cultures revealed the presence of a short bacillus resembling the bacterium *lactis aerogenes* of Escherich. Pure cultures injected into the tissues of animals always resulted in gas formation.

Schnitzler (*Internationale klinische Rundschau*, February 25, 1894) reports an analogous case in a woman forty-six years old, the only difference being that the catheter had never been used. Here, also, the formation of gas was due to the presence of the bacillus *lactis aerogenes*. The author made experiments with the bacillus *coli* for the purpose of showing its gas-producing effect, but only succeeded in animals he had first rendered diabetic by phloridzin. In the same way the injection of the bacillus *lactis aerogenes* produced violent cystitis, but developed gas only in animals rendered diabetic. These experiments show that decomposition of urea and putrefaction caused by microbes is often greatly influenced by the composition of the urine. Saprophytic infection is almost always associated with urine retention, and may precede or follow infection with the microbes which are the essential cause of the suppurative cystitis. It is in such cases that careful, systematic catheterization and antiseptic irrigations of the bladder prove of such eminent value in correcting the alkalinity of the urine and in arresting the suppurative inflammation.

(c) *Staphylococcus Infection*.—The staphylococcus *pyogenes albus* and *aureus*, the microbe most frequently found in all suppurative affections has been often demonstrated as a solitary microbe, and in association with other pyogenic microbes and saprophytic bacteria in the urine of patients suffering from catarrhal and suppurative cystitis. The staphylococcus is a comparatively mild microbe, and its presence as a sole microbial cause should be suspected in inflammatory affections of the bladder in which the infection does not penetrate deeply, and in which the urine shows no evidences of exfoliation. In staphylococcus infection the urine may be ammoniacal without the presence of saprophytic bacteria, as pus microbes, when present in large numbers, decompose the urea, besides lighting up the suppurative inflammation.

(d) *Streptococcus Infection*.—That the streptococcus *pyogenes* is not often the cause of cystitis becomes apparent from a bacteriological examination of the urine from six cases of inflammation of the bladder made by Huber (*Correspondenzblatt für Schweizer*

*Aerzte*, October, 1893). He found this microbe only once; in the remaining five cases the bacillus coli commune.

Melchior found the urine acid in all cases of cystitis in which the streptococcus was found as a solitary microbe. It is well known that the streptococcus generally produces a diffuse form of inflammation, during which the connective tissue is often destroyed by the toxins and is later eliminated or removed in the form of shreds. The streptococcus invades the lymphatic channels and connective tissue spaces, and is almost constantly found in phlegmonous inflammations and diffuse abscesses. A streptococcus cystitis is characterized by the intensity of the local and general symptoms and by more or less destruction of the tissues of the bladder wall. The presence of this microbe may be surmised in cases of diffuse interstitial and exfoliative cystitis.

(e) *Erysipelatous Cystitis*.—Erysipelatous inflammation, either as a primary affection or as a metastatic process, has been found in many of the internal organs. Infection of the bladder with the streptococcus erysipelatis is extremely rare, but there can be no doubt of the possibility of such an occurrence.

Fritsch (*Centralblatt für Chirurgie*, 1894, No. 7) reports the case of a man, aged fifty-two, suffering for a long time from symptoms of suppurative prostatitis, and who was attacked with chills, fever, vomiting, and frequent desire to urinate; the urine, very turbid, contained streptococci, as did also the mucopurulent secretions of the prostate. The erysipelatous character of the cystitis was demonstrated by culture and inoculation experiments. The patient suffered subsequently from an erysipelas of the left thigh, which extended to the right thigh, the back, etc., but eventually he recovered.

(f) *Typhoid Infection*.—Our distinguished member, Professor W. W. Keen, has recently made a most important addition to the literature pertaining to typhoid infection and complications in his classical book on "The Surgery of Typhoid Fever." He mentions a number of cases of typhoid infection of the male and female genital organs, but nothing is said of cystitis as a possible complication or remote consequence of typhoid fever.

Melchior ("Om Cystitis og Urininfection," etc.) reported the first and probably the only case of cystitis caused by infection with the typhoid bacillus. The patient had been convalescent from an

attack of typical typhoid fever for fourteen days, and had been out of bed for three days, when he was attacked suddenly with a severe form of cystitis, for which there appeared to be no cause, as the catheter had never been used. For several days the urine was sterile, and contained a large amount of pus and some blood. The typhoid bacillus was cultivated from the urine, and was the only microbe it contained. In rabbits injections of pure cultures into the bladder obstructed for eighteen hours by ligation of the penis caused a severe cystitis. Intravenous injections caused death of the animals from typhoid fever with the characteristic anatomical lesions.

(g) *Diplobacillus Infection*.—The diplobacillus of Friedländer, which has been found in so many suppurative lesions complicating or following pneumonia, has in rare instances been found as the only microbic cause of cystitis. In a case of general infection with this microbe which resulted in death, Brunner (*Münchener medicinische Wochenschrift*, Nos. 13, 14, 1896) found at the post-mortem, besides other multiple lesions, hemorrhagic lesions.

Montt-Saverdo ("Zwei Fälle von Cystitis mit Befund von Diplobacillus," Friedländer, *Centralblatt für Bacteriologie*, etc., Band xx., Nos. 4, 5, 1896) found the diplobacillus of Friedländer in the urine of two cases of cystitis, which, in the absence of other microbes, was regarded by him as the essential cause of the disease. The first patient was a man fifty-three years of age who three years previously suffered from an attack of pneumonia. For two months he had been the subject of cystitis characterized by the escape of gas from the urethra. The urine contained pus, small quantity of albumen and diplobacilli, but no gonococci. In the second case the suppurative cystitis was complicated by hypertrophy of the prostate. The symptoms yielded to washings out of the bladder with solutions of salol and nitrate of silver. Five years later there was a return of the cystitis, with phlebitis of the saphenous vein and death, preceded by septic manifestations. The autopsy revealed carcinoma of the prostate and conditions indicated by the clinical course of the disease, also a few bronchopneumonic foci. Bacteriological examination of the urine resulted in the finding of staphylococcus pyogenes and the diplobacillus of Friedländer.

(h) *Gonococcus Infection*.—It has been said that the gonococcus never causes cystitis, and that a gonorrhœal urethritis, as long as it



remains as an unmixed infection, does not extend to the bladder. It is claimed that when cystitis develops in the course of a specific urethritis it is the result of a mixed infection. This is undoubtedly true in the majority of cases, but occasionally a gonorrhœal cystitis is met with in which the gonococcus is found as a solitary microbe in the urine. It is not always easy to demonstrate the gonococcus in the urine in gonorrhœal cystitis. The reason why gonococci are not always found in the chronic cases, as Wertheim has pointed out, is that, while young gonococci are well stained with aqueous solutions of anilin colors, the old germs are pale and imperfectly defined. Moreover, gonococci assume "involution forms," becoming granular and of irregular form when the culture medium becomes old. These forms are not recognizable as gonococci, yet they can be regenerated to the classical form through a fresh culture medium. Gonorrhœal cystitis presents itself more frequently in the form of a localized than a diffuse inflammation of the bladder. The favorite location for this form of cystitis is the trigonum of the bladder. If the disease becomes more diffuse, it manifests a tendency to extend in the direction of the kidneys. The most conclusive proof of the existence of gonorrhœal cystitis has been furnished by Wertheim ("Ueber Blasengonorrhöa," *Zeitschrift für Geburtshülfe*, Band xxxv., Heft 1). In a girl nine years of age, suffering from gonorrhœal cystitis, he excised, with the aid of the cystoscope, a piece of the mucous membrane of the bladder, in which he found an abundance of gonococci in the tissues of the specimen removed; some of the gonococci were seen between the epithelial cells; some had penetrated deeper into the vessels where they had produced gonorrhœal thrombosis in the capillaries and veins.

(i) *Tubercular Cystitis*.—Tubercular cystitis furnishes the best clinical representation of chronic cystitis. With few exceptions, a primary chronic cystitis is of a tubercular nature. It is important to bear this in mind in the examination of all cases of cystitis in which the initial symptoms point to a chronic inflammatory process.

Tuberculosis of the bladder is caused either by infection with the bacillus of tuberculosis through the blood, by extension of a tubercular process by continuity of surface from the kidney or the genital organs, or by the rupture of a tubercular abscess into the bladder. Vesical tuberculosis is found more frequently in males than in females, and is usually a disease of early and middle life. Tuber-

culosis of the bladder in the male is generally associated with a similar affection of the seminal vesicles and prostate. Localization of tubercle bacilli in the mucous membrane of the bladder, like that of pyogenic and saprophytic bacteria, is favored by antecedent affections of the urinary tract. Primary tuberculosis from infection through the blood is so rare that König doubts its existence. Infection takes place most frequently from the kidneys; less frequently from the prostate, seminal vesicles, and epididymis. The resistance of the mucous membrane of the bladder to tubercle bacilli is great. In many cases tuberculosis of the kidneys may exist for several years without affecting the bladder. The mucous membrane of the bladder can be irrigated with urine containing tubercle bacilli for years without becoming tubercular. Clado pointed out that tubercular granulations in the bladder do not, as is claimed by some authors, occupy the submucous tissue, but the mucous membrane itself,—that is, the subepithelial layer. He believes that this is due to the presence of a well-developed capillary net-work in the mucous membrane, which determines localization of the bacilli floating in the general circulation. Secondary infection occurs most frequently from the prostate or the kidneys, and least frequently as a result of an ascending tubercular affection of the testicles. In other cases the bladder is involved by the rupture into it of a tubercular prostatic abscess, or by the extension along the ducts to the urethra, and from there to the bladder. An ascending tuberculosis of the ejaculatory ducts in other cases precedes the bladder affection. A previous gonorrhoeal cystitis not infrequently prepares the soil for tubercular infection. König observed a case in which a turpentine intoxication first produced active symptoms in a case of latent catarrhal tubercular cystitis caused by a tubercular kidney.

Although no age is exempt, tuberculosis of the bladder occurs most frequently in men between seventeen and forty years of age. Baudet records a case in a boy fifteen years old; in this case the earliest point of invasion, so far as could be determined, was the testicle, then the prostate and bladder, thence along the ureter to the kidney. The writer has seen, in a girl nine years of age, a case of primary vesical tuberculosis that extended to both kidneys and proved fatal in less than a year.

The two places in which tuberculosis of the bladder is most likely to commence are the ureteral orifices and the trigone of the

bladder. The former starting-point of the disease is the rule when the bladder becomes involved by a descending tubercular ureteritis,—that is, when the disease is secondary to renal tuberculosis; the trigone is usually the original seat of the disease in primary tuberculosis of the bladder, and in men also by the extension of the disease from the genital organs.

The tubercular disease here as elsewhere is characterized by the same chain of pathological changes,—infiltration, caseation, and ulceration. Penetration of the bladder wall frequently leads to the formation of perivesical abscess and fistula formation, a part or all of the urine escaping through the fistulous opening. The chronic inflammation and the vesical tenesmus lead to great thickening of the wall of the bladder, sacculation, and diminished capacity of the organ. The extension of the tubercular inflammation over the surface and in the direction of the different tunics of the bladder wall is hastened in case the bladder becomes infected with pus microbes, which is so often the case, and which is so frequently caused by the needless use of instruments in the fruitless search for stone in the bladder, which a beginning vesical tuberculosis often mimics so closely. The complications most frequently encountered in post-mortem examinations of patients who have died of the direct or indirect effects of tuberculosis of the bladder are tuberculosis of the lungs, kidneys, genital organs, and peritoneum, and perivesical tubercular abscesses with or without fistula formation. The disease is initiated by a frequent desire to urinate and by pain after emptying the bladder, with slight hæmaturia at longer or shorter intervals. Urination becomes more frequent as the disease advances, and after the neck of the bladder has been reached incontinence of urine becomes a conspicuous clinical symptom. The urine exhibits the same appearance and contains the same morphological constituents during the early stages of the disease as in cases of chronic catarrh of the bladder. In the beginning of the disease the urine is acid and contains pus, bladder epithelia, and a small quantity of albumen. If the kidneys are affected at the same time, the albumen is more abundant. If secondary infection with pus microbes or saprophytic bacteria has occurred, it is alkaline in reaction and often ammoniacal, and then contains also a larger amount of mucus and pus-corpuscles and disintegrated red blood-corpuscles, besides the large flat epithelial cells from the bladder. As soon as the cheesy material on



the surface of the bladder softens and disintegrates, fragments of detritus are found in the urine. Tubercle bacilli are not always present, and their detection is often very difficult. Their presence can also be determined by cultivation on artificial nutrient media and by inoculation experiments. If, in cases of suspected bladder tuberculosis, the bacillus cannot be found, the injection of a few drops of the urine sediment into the eye, a joint, the pleura, or the peritoneal cavity of a rabbit or a guinea-pig, will often succeed in reproducing the disease, and upon the results of such experiments we must then base our diagnosis. The positive results of such experiments and the detection of bacilli in the urine do not enable us always to locate the disease anatomically; in other words, we must ascertain further whether the disease involves the kidney, the bladder, or the lowest portion of the urinary tract. Nitze's cystoscope is a useful diagnostic instrument in the hands of experts. Finally, it may be stated that in all chronic inflammatory affections of the urinary organs it is necessary to make careful and often repeated examinations, both of the general and local symptoms, for the purpose of locating the disease, as well as to determine its nature, which often can be done in a satisfactory manner only by making a microscopical and bacteriological examination of the urine. If this should still leave the diagnosis doubtful, a resort to inoculation experiments upon animals susceptible to tuberculosis becomes necessary as a decisive diagnostic test.







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EDITED BY

JUDSON DALAND, M.D.,

Philadelphia, Pa.

J. MITCHELL BRUCE, M.D., F.R.C.P.,

London, England.

DAVID W. FINLAY, M.D., F.R.C.P.,

Aberdeen, Scotland.

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